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AP/JPW

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Konduri, et al
Serial No.: 10/769,661 034
Filed: 01/30/04
Examiner: Kevin K. Hill
For: Art Unit: 1633
Docket No.: KSKO-25,661

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Date of Deposit: 7-19-07

F. Lindsey Scott
Signature of Person Mailing Document(s)

For: A Sterically Stabilized Carrier for
Aerosol Therapeutics, Compositions
and Methods For Treating Diseases of
the Respiratory Tract of a Mammal

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Enclosed is a Credit Card Payment Form for the amount of \$250.00 in payment of the fee for filing this Brief on Appeal.

Three copies of the Brief on Appeal are attached hereto.

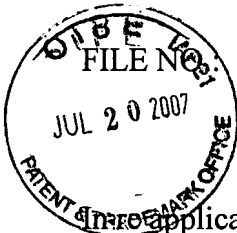
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KSKO-25,661

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Kameswari S. Konduri, et al
Serial No.: 10/769,034
Filed: 01/30/04
Group Art Unit:
Examiner: Kevin K. Hill

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail in an envelope addressed to Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450.

Name: *J. Lindsey Scott*
Date: *7-20-07*

For: A Sterically Stabilized Carrier for Aerosol Therapeutics, Compositions and Methods For Treating Diseases of the Respiratory Tract of a Mammal

MS Board of Appeals
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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BRIEF ON APPEAL

Pursuant to a Notice of Appeal filed May 29, 2007, Applicants set forth herein the authorities and arguments upon which Applicants rely. By separate Transmittal Letter filed herewith Applicants have enclosed a Credit Card Payment Form for \$250.00 in payment of the fee for filing this brief in support of an appeal. Please credit any overpayment or charge any additional fees due for this Brief on Appeal to Deposit Account 50-0232

REAL PARTY IN INTEREST

This Application is assigned to VGSK Technologies, Inc., the real party in interest, by an assignment recorded April 11, 2006 at Real/Frame 017856/0582.

STATUS OF CLAIMS

The subject application was filed initially as U.S. Serial No. 10/769,034 on January 30, 2004 by Kameswari S. Konduri, Sandhya Nandedkar, Nejat Duzgunes, Pattisapu Ram Jogi Gangadharma (deceased) by Ramarrishna Pattisapu, his legal representative. The application claimed the benefit of provisional application serial no. 60/498,609 filed August 28, 2003 and the benefit of provisional application serial no. 60/498,546 filed August 28, 2003. The application as originally filed contained 52 claims of which claims 1, 18 and 34 were independent.

In a first Office Action mailed May 2, 2006, Applicants' claims were held subject to a restriction requirement (copy attached). Applicants were unable to understand what restriction was desired by the Examiner and a telephonic interview was held May 19, 2006 with Examiner Kevin K.

Adjustment date: 07/24/2007 EAYALEW1
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Hill, Dr. Kameswari S. Konduri and attorney for the Applicants, F. Lindsey Scott to clarify the restriction requirement. It was ultimately agreed by the parties that Applicants would limit their application to a single drug, i.e., budesonide, for examination.

An Office Action dated August 10, 2006 was issued wherein Applicants' claims 1-52 were considered and wherein Applicants' claims 6, 28 and 52 were withdrawn and claims 1-5, 7-27 and 29-51 were rejected, with claim 30 being objected to.

The rejections were based upon the restriction requirement, with the Examiner stating that the drugs are each independent and mutually exclusive of the others, objections made under 35 U.S.C. 112 with respect to an alleged failure to point out and specifically claim the subject matter considered by Applicants to be the invention (assertion of "does not reasonably provide enablement for all possible formulations"), rejection under 35 U.S.C. 102 of claims 1-4, 7-14, 16-27, 29-31, 33-34 over Onyuksel, et al, (herein Onyuksel), U.S. Patent 6,197,333B1 issued March 6, 2001. Separate claim rejections were made over Onyuksel of claims 1, 2, 14, 18-19 and 31 and claims 3-4, 9-12, 16-17, 20-23 and 33-34 and claims 7-8, 24-27 and 29 and claims 13 and 30. Claims 1, 5, 14-15, 18, 31-32 and 35-51 were rejected under 35 U.S.C. 103(a) over Waldrep, et al (herein Waldrep), U.S. Patent 5,958,378 as applied to the limitation of a liposome carrier and the drug budesonide further in view of Onyuksel and a medical journal abstract by Konduri, et al (herein Konduri), J. Allergy Clin. Immunology Supp. 107(2): S315, 2001 and Waldrep (Abstract Only) Drugs Today, 34(6):549561, 1998.

Applicants responded to this Office Action with an amendment mailed December 5, 2006 wherein Applicants limited the claims to claims 1-4, 8-13, 16-19, 22-27, 29-30, 33-39, 42-46, 49 and 50. Various amendments were made to the claims to overcome various formal rejections. Various objections raised by the Examiner with respect to the breadth of support were addressed. Also the formal correspondence of the claims to the specification were addressed.

A Notice of a Non-Compliant Amendment was mailed November 28, 2006 and Applicants thereafter responded to this Notice December 5, 2006 with an attempt to bring the amendment into compliance.

A final rejection was made in an Office Action mailed March 1, 2007, wherein Applicants' claims 1-6, 8-19, 22-30, 33-39, 42-50, 52 and 53 were considered. Applicants claims 1-5, 8-13, 16-19, 22-29, 32-38, 41-45, 48-49 and 52 were rejected with claims 4, 13, and 45 being objected to.

The Examiner raised numerous formal objections, varying from disagreement with Applicants' spelling of certain of the compounds to a request to renumber the claims due to a missing claim 28, and a requirement for the filing of a Terminal Disclaimer for a non-elected claims with respect to U.S. Serial No. 11/442,907 which is directed to the carrier alone.. Claim rejections were also made under 35 U.S.C. 112, first paragraph, based upon an allegation that Applicants had not provided enablement for "all possible formulations." Various other arguments were made by the Examiner with respect to the state of the art, level of ordinary skill in the art, etc., all directed to the premise that Applicants have not disclosed sufficient detail to enable those skilled in the art to duplicate Applicants' claimed invention. Among other arguments made by the Examiner in this Office Action was the argument that "The drug carried by the liposome is immaterial to the enablement rejection." This statement was made after the restriction requirement to a single drug was required by the Examiner. Various other arguments were raised with respect to support in the application for various claims and additional rejections under 35 U.S.C. 112 were made.

Rejections were made under 35 U.S.C. 102 over Onyuksel. Rejections were made under 35 U.S.C. 103 over Onyuksel, Waldrep and Konduri, et al.

A response to this Office Action was mailed to the Patent Office July 19, 2007 with a request for a two-month extension of time to file.

STATUS OF AMENDMENTS

Applicants' claims as amended in the response to the Final Office Action mailed March 1, 2007, are currently pending in this application and a copy is attached hereto. This amendment was mailed July 19, 2007 and is currently pending before the Patent Office.

If the Amendment is entered, the claims under appeal will be the claims 1-3, 8-13, 16-29, 24-27, 29-30, 33-35, 42-46, 49-50 (using claim numbers as originally filed and as referred to by Applicants herein. If the Examiner's numbering system is used, the claim numbers are 1-3, 81-3, 16-19, 24-27, 28-29, 32-34, 41-45 and 48-49. These claims presently stand finally rejected.

SUMMARY OF THE INVENTION

The claimed invention is a carrier comprising phosphatidylglycerol, phosphatidylcholine, and poly(ethylene glycol) adapted to encapsulate a drug for administration to the lungs of a mammal. The formulation comprising the carrier and the drug provide extended effective life for the drug in the lungs of a mammal. The invention is claimed as a carrier formulation, a composition

comprising the carrier and an encapsulated drug, and a method for treating the lungs of a mammal using the combined drug and carrier.

ISSUES

Is Applicants' spelling and hyphenation of chemical compounds as amended acceptable? This issue has been addressed in the amendment filed July 19, 2007 and is believed to have been obviated by the changes therein.

Is a double patenting rejection proper based upon U.S. Patent Application 11/442,907? If the amendment after final, including the required terminal disclaimer, is entered does this issue become moot?

Do Applicants claims 34-38, 41-45 and 48-49 (Examiner's new numbering), rejected under 35 U.S.C. 112 on the basis that they do not provide enablement for "all possible formulations" meet the disclosure and enablement requirements of 35 U.S.C. 112?

Do claims 3-5, 9-11, 22, 27, 35, 37-38, 42-43 and 52, rejected under 35 U.S.C. 112, meet the requirements of 35 U.S.C. 112?

Do claims 3-5, 23-26, 35 and 52, separately rejected under 35 U.S.C. 112 meet the requirements of 35 U.S.C. 112?

Are Applicants' claims patentable under 35 U.S.C. 102 in view of Onyuksel?

Are Applicants' claims patentable under 35 U.S.C. 103 over Onyuksel, Waldrep and Konduri?

GROUPING OF CLAIMS

Claims 1-3, 8-13 and 16-17 (Applicants' numbering) stand or fall as a group.

Claims 18-19, 24-27, 29-30 and 33-34 (Applicants' numbering) stand or fall as a group.

Claims 42-46 and 49-50 (Applicants' numbering) stand or fall as a group.

ARGUMENT

It is considered that Applicants' amendments to the specification and claims with respect to spelling and hyphenation of chemical compounds, as corrected in the July 19, 2007 amendment has obviated all rejection to these matters.

It is further submitted that unless an objection is raised or unless the amendment after final is denied entry, it appears that the double patenting rejection, which Applicants consider to be improper, has been fully obviated by Applicants' required submission of a Terminal Disclaimer with the amendment dated July 19, 2007.

The Examiner's requirement for renumbering of the claims has resulted in considerable superficial confusion. The rejections are stated accordingly in the Examiner's numbers, but Applicants' listing of pending claims and Applicants' claim groups are stated in Applicant's numbers which correspond to the numbers as originally filed.

The rejection of Applicants' claims under 35 U.S.C. 112 is primarily based upon the Examiner's position that the disclosure in Applicants' disclosure does not provide enablement for "all possible formulations" It is respectfully submitted, particularly in view of the Examiner's comments in other places in the Office Action, that the drug is considered to be "immaterial." It is Applicants' position that having disclosed a sterically stabilized liposome formulation which is compatible with the lungs of a mammal and which encapsulates a drug is sufficient to enable those skilled in the art to produce suitable carrier materials. Applicants are unaware of any third party having used sterically stabilized liposomes as a carrier in the lungs of a mammal prior to Applicants' use as disclosed in the subject application. The surfactants found in the lung of a mammal are known and may vary from one mammal to another. Applicants have disclosed the use of budesonide as a drug in the examples to show the extended results achieved by encapsulating drugs in Applicants' carriers. It is not considered to be the law that all possible formulations must be enabled specifically. It is respectfully submitted that suitable formulations can be produced by those skilled in the art based upon their knowledge of the conditions in the lungs of a mammal based upon Applicants' disclosure and examples.

The Examiner has speculated at length as to whether experimentation or testing is necessary. Some experimentation is permissible to define the effectiveness of a compound. In other words, if a compound is produced which is not compatible with the lungs of a particular mammal to which it is administered, it is possible that the desirable results may not be achieved. There is certainly nothing, however, which prevents those skilled in the art from reviewing the properties of their produced carrier by comparison to the lung surfactants in the mammal of interest to produce an effective carrier. It is noteworthy that the Examiner has stated on page 11 of his relatively lengthy office action that, "The drug carried by the liposome is immaterial to the enablement rejection." This is a strange position for an Examiner to take after requiring restriction to a single drug. This previously required restriction to a single drug could result in Applicants having to file as many as 30 to 50 applications directed to specific separate drugs to fully protect their invention. It is not considered that this is the law.

The Examiner further opines that one of ordinary skill in the art cannot reasonably extrapolate Applicants' disclosure of a single liposome formulation to an entire genus of liposome formulations and expect that all possible formulations and species embraced by the genus will perform according to the inventive method. It is well known that there are many liposome and sterically stabilized liposome formulations. Liposomes have been used for many intravenous treatments. These sterically stabilized liposomes for intravenous treatments can very well have properties which would not be suitable for use in the lungs of a mammal. It is considered that those skilled in the art can determine the conditions for compatibility with the lungs of a selected mammal and can formulate their sterically stabilized liposome formulations accordingly.

The Examiner's discussion on pages 14 and 15 directed to the proper spelling of the materials is believed obviated by the amendment filed July 19, 2007.

The rejection of Applicants' claims 1, 5, 8-13 and 16-17 under 35 U.S.C. 102(b) as anticipated by Onyuksel is respectfully traversed and reconsideration is respectfully requested. Applicants' claims are drawn to a composition comprising a sterically stabilized liposome carrier for encapsulating a drug. It is noted that the carrier encapsulates the drug, unlike Onyuksel. Onyuksel discloses various formulation techniques for the production of his materials, which are claimed as sterically stabilized liposomes which are formed and thereafter contacted with, blended with, or combined with an amphipathic compound. These materials include many combinations of liposomes with a variety of water-soluble polymers for purposes of producing sterically stabilized liposomes, many of which are considered unsuitable by Applicants. Onyuksel speculates that his liposomes may be effective for treating a variety of diseases, such as asthma, and that the disclosed compositions may be delivered by aerosol administration, nebulization, etc. It is respectfully pointed out that Onyuksel does not show any way (enablement) for treating asthma with any drugs or carriers or any combinations thereof disclosed in his patent disclosure or that any such treatments would be effective. Further no technique or formulation is shown for administration, nebulization, etc. Accordingly, these are simply speculations and attempts to broadly cover a much wider area than encompassed in Onyuksel's disclosure.

Onyuksel basically claims the use of sterically stabilized liposomes to produce sterically stabilized liposomes to support an amphipathic compound which is much beyond the scope or enablement of his disclosure. The disclosure is limited to peptides of various types. Onyuksel discloses as column 16 a method which is not the same as Applicants' preferred method, which

requires drug encapsulation and includes some additional steps. This is disclosed as a method for mixing the VIP with a lipid composition followed by extrusion, repeated freezing and thawing, etc. The difference between this technique and the other techniques which are considered to be within the scope of Onyuksel's invention is that in this instance the VIP was initially mixed with the lipids for the production of an encapsulated amphipathic material encapsulated in the sterically stabilized lipids.

It is indicated at column 17, lines 42-43 that the lipids, the VIP and liposomes prepared by the first method, which is outside the scope of the invention, did not elicit an increase in arterial diameter significantly different than previously reported. It is also noted in this same paragraph that when liposomes are produced without an extrusion step they show an enhanced prolonged effect and that further the result is significant in demonstrating that SSL (sterically stabilized liposomes) in general are not amenable to the present invention. This is directly contrary to Applicants' results with the claimed carrier and encapsulation of the drug in the carrier.

Further it is noted that Onyuksel obtained very slight increases in effective life with the longest persistence of effect noted being at column 18, lines 9-13 wherein a significant decrease in mean arterial pressure, up to 50%, was observed in the first 2.5 hours which persisted for the sixth hour observation. Onyuksel, then has not achieved anything approaching the extended effective life for the drug achieved by Applicants.

Onyuksel's formulations do not encapsulate the drug but rather blend the drug with the formed sterically stabilized liposomes for use in a treatment. It is Applicants' position that this does not encapsulate the drug in the carrier and would not be expected to provide extended effectiveness for the drug.

Further Onyuksel is extremely vague in the types of material used and it is not possible to determine from the specification whether these materials might be suitable for use in the lungs of a mammal. Onyuksel also does not disclose the use of the drug required by restriction in the subject application for use with a sterically stabilized liposome carrier.

Further the Examiner's position has been that the preparation of sterically stabilized liposomes was well known long before the Onyuksel disclosure. Such is the case. However, a wide variety of sterically stabilized liposomes can be prepared, some of which are more suitable for use intravenously and some which are suitable for other purposes. There is no suggestion in Onyuksel

that sterically stabilized liposomes compatible with the lungs of a mammal should be produced or used.

Applicants' claims 1, 5, 14-15, 18, 30-31 and 34-50 have been rejected under 35 U.S.C. 103 based upon Konduri and Waldrep. Konduri discloses in the Abstract that sterically stabilized liposomes with budesonide are effective to obtain an extended effective life of a drug. There is no suggestion as to the particular type of sterically stabilized liposomes which should be used, how they should be prepared or that they would be effective with any other drug. The Konduri reference has been combined with Waldrep, which is apparently cited to support the premise that large amounts of drugs can be used with liposome treatments. The liposomes in Waldrep used do not appear to be sterically stabilized liposomes. In Applicants' examples, it is shown that non-sterically stabilized liposomes combined with budesonide were not effective. Thus, the argued combination of these two references results in a disclosure of a technique and compound which has been demonstrated to be non-effective. Nothing in Waldrep suggests that sterically stabilized liposomes should be used. Konduri does not suggest that suitable sterically stabilized liposomes should be used in Waldrep in lieu of the non-sterically stabilized liposomes disclosed cited in Waldrep. Accordingly, there is no reason to combine these references. Even if combined, these references do nothing to show or suggest Applicant's claimed invention.

Claims 1 and 2, 5, 8-13, 16-17 and 52 have been rejected under 35 U.S.C. 103(a) in a rejection noted by the Examiner as "new rejected." This seems counterintuitive to the requirement that the prosecution be completed before a final rejection is made. In other words, Applicants have had no opportunity to respond to this rejection prior to receiving notice that it had been "newly" made in a final rejection mailed March 1, 2007.

In any event, Onyuksel is not considered to show or suggest Applicants' claimed invention as discussed above and actually is considered to teach away from Applicants' claimed invention. Waldrep does nothing to add to the disclosure in Onyuksel since a different type of liposomes are used and Konduri is not considered to show or suggest any specific sterically stabilized liposomes which would be effective to achieve the desired objective.

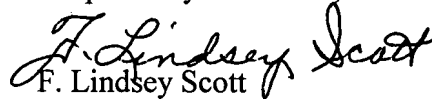
Claims 18-19, 22-27, 28-29, 32-38, 41-45 and 48-49 have also been "newly" rejected under 35 U.S.C. 103(a) in a final rejection. These claims are directed to substantially the same issues and are not considered to be shown or suggested by any of the references cited above.

In view of the foregoing amendments and comments, it is respectfully submitted that none of Applicant's claims fail to comply with 35 U.S.C. 112, that the enablement requirements under 35 U.S.C. 112 are met, that none of Applicants' claims have been shown by Onyuksel and that none of Applicants' claims have been shown or suggested under 35 U.S.C. 103 by the cited references.

Accordingly, it is respectfully requested that the Examiner be reversed and that Applicants' claims be passed to issue.

In the event that the Examiner fails to enter the amendment mailed July 19, 2007 or in the event that the Examiner makes still more additional new objections or rejections in response to the amendment of July 19, 2007 it is respectfully requested that Applicants be permitted to respond to any new grounds as appropriate within the scope of this Appeal.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "F. Lindsey Scott", written in a cursive style.

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Attorney for the Applicants
Registration No. 26,230

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Appealed Claims

1. A sterically stabilized liposome carrier wherein the carrier contains phosphatidylcholine, phosphatidylglycerol and poly(ethylene glycol), the carrier encapsulating budesonide for aerosol administration, the carrier being compatible with a respiratory tract of a mammal and effective to extend the effective life of the budesonide in the respiratory tract by a time equal to at least twice the effective life of the budesonide alone.
2. The carrier of claim 1 wherein the time is equal to at least three times the effective life of the budesonide alone.
3. The carrier of claim 1 wherein the carrier contains phosphatidylcholine in an amount up to 99% of the total phosphatidylcholine and phosphatidylglycerol in the carrier.
4. (cancelled).
5. (cancelled)
6. (cancelled)
7. (cancelled)
8. The carrier of claim 1 wherein the poly(ethylene glycol) has a molecular weight from about 500 to about 5,000 daltons.
9. The carrier of claim 1 wherein poly(ethylene glycol) is attached to lipids such as cholesterol or phosphatidylethanolamine having acyl chains containing from about 8 to about 18 carbon atoms.
10. The carrier of claim 9 wherein the acyl chains contain from about 16 to about 18 carbon atoms.
11. The carrier of claim 9 wherein the acyl groups comprise at least one of distearoyl, stearoyl oleoyl, oleoyl stearoyl, stearoyl palmitoyl, dipalmitoyl, dioleoyl, palmitoyl oleoyl and dipalmitoleoyl.
12. The carrier of claim 1 wherein the carrier comprises at least one of poly(ethylene glycol) conjugated lipids, phosphatidylinositol, dipalmitoylphosphatidylpolyglycerol, lipid conjugated polyoxyethylene, lipid conjugated polysorbate, or lipids conjugated to other hydrophilic steric coating molecules safe for in

vivo use, the sterically stabilized liposome being effective to extend the effective lifetime of the budesonide in the respiratory tract of a mammal.

13. The carrier of claim 1 wherein the carrier contains phosphatidylcholine and phosphatidylglycerol, poly(ethylene glycol) distearylphosphatidyl diethanolamine, with or without cholesterol.

14. (cancelled)

15. (cancelled)

16. The carrier of claim 1 wherein the carrier comprises egg-derived or soybean-derived phosphatidylcholine.

17. The carrier of claim 1 wherein the carrier comprises egg-derived or soybean-derived phosphatidylglycerol.

18. A composition comprising a sterically stabilized liposome carrier wherein the carrier contains phosphatidylcholine, phosphatidylglycerol and poly(ethylene glycol) encapsulating budesonide, the composition being compatible with a respiratory tract of a mammal, aerosol administration and effective to extend the effective life of the budesonide in the respiratory tract by a time equal to at least twice the effective life of the budesonide alone.

19. The composition of claim 18 wherein the time is equal to at least three times the effective life of the budesonide alone.

20. (cancelled)

21. (cancelled)

22. (cancelled)

23. (cancelled)

24. The composition of claim 20 wherein the carrier further comprises poly(ethylene glycol).

25. The composition of claim 24 wherein the poly(ethylene glycol) has a molecular weight from about 500 to about 5,000 Daltons.

26. The composition of claim 18 wherein at least one of phosphatidylcholine, phosphatidylglycerol or poly(ethylene glycol)-derivatized lipid have acyl chains containing from about 8 to about 18 carbon atoms.

27. The composition of claim 26 wherein the acyl groups comprise at least one of distearoyl, stearoyl oleoyl, oleoyl stearoyl, stearoyl palmitoyl, dipalmitoyl, dioleoyl, palmitoyl oleoyl and dipalmitoleoyl.

28. (cancelled)

29. The composition of claim 18 wherein the carrier comprises at least one of poly(ethylene glycol) conjugated lipids, phosphatidylinositol, dipalmitoylphosphatidylpolyglycerol, lipid conjugated polyoxyethylene, lipid conjugated polysorbate, or lipids conjugated other hydrophilic steric coating molecules safe for in vivo use, the sterically stabilized liposome being effective to extend the effective lifetime of budesonide in the respiratory tract of a mammal.

30. The composition of claim 18 wherein the carrier contains phosphatidylcholine, phosphatidylglycerol, and poly(ethylene glycol) distearylphosphatidyl diethanolamine.

31. (cancelled)

32. (cancelled)

33. The composition of claim 18 wherein the carrier comprises egg-derived or soybean-derived phosphatidylcholine.

34. The composition of claim 18 wherein the carrier comprises egg-derived or soybean-derived phosphatidylglycerol.

35. A method for treating the respiratory tract of a mammal by aerosol administration of an effective amount of a composition comprising a sterically stabilized liposome carrier wherein the carrier contains phosphatidylcholine, phosphatidylglycerol and poly(ethylene glycol) with the carrier encapsulating budesonide, the sterically stabilized liposome being compatible with the respiratory tract of a mammal and effective to extend the effective life of the budesonide in the respiratory tract by a time equal to at least twice the effective life of the budesonide alone.

36. (cancelled)

37. (cancelled)

38. (cancelled)

39. (cancelled)

40. (cancelled)
41. (cancelled)
42. The method of claim 35 wherein the poly(ethylene glycol) is attached to a lipid such as phosphatidylethanolamine and has acyl chains containing from about 8 to about 18 carbon atoms.
43. The method of claim 42 wherein the acyl chains contain from about 16 to about 18 carbon atoms.
44. The method of claim 42 wherein the acyl groups comprise at least one of distearoyl, stearoyl oleoyl, oleoyl stearoyl, stearoyl palmitoyl, dipalmitoyl, dioleoyl, palmitoyl oleoyl and dipalmitoleoyl.
45. The method of claim 35 wherein the carrier comprises at least one of poly(ethylene glycol) conjugated lipids, phosphatidylinositol, dipalmitoylphosphatidylpolyglycerol, lipid conjugated polyoxyethylene, lipid conjugated polysorbate, or lipids conjugated other hydrophilic steric coating molecules safe for in vivo use, the sterically stabilized liposome being effective to extend the effective lifetime of a drug in the respiratory tract of a mammal.
46. The method of claim 35 wherein the carrier contains phosphatidylcholine, phosphatidylglycerol, and poly(ethylene glycol) distearylphosphatidyl diethanolamine, with or without cholesterol.
47. (cancelled)
48. (cancelled)
49. The method of claim 35 wherein the carrier contains egg-derived or soybean-derived phosphatidylglycerol.
50. The method of claim 35 wherein the carrier contains egg-derived or soybean-derived phosphatidylglycerol.
51. (cancelled)
52. (cancelled)
53. (cancelled)



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/769,034

01/30/2004

Kameswari S. Konduri

KSKO-25,661

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05/02/2006

EXAMINER

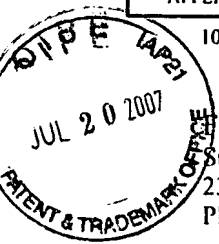
HILL, KEVIN KAI

ART UNIT

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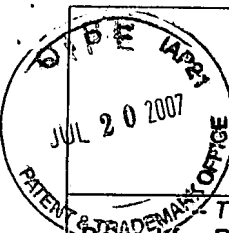
1633

DATE MAILED: 05/02/2006



Ms. Lindsey Scott
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Plano, TX 75075

Please find below and/or attached an Office communication concerning this application or proceeding.



Office Action Summary

Application No.	Applicant(s)	
10/769,034	KONDURI ET AL.	
Examiner	Art Unit	
Kevin K. Hill, Ph.D.	1633	

The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133) Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☐ This action is FINAL.
- 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-52 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s)-including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some * c) ☐ None of:
 - 1. ☐ Certified copies of the priority documents have been received.
 - 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date: _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Examiner Notes

Claims 8 and 25 are self-referential. Amendment to claim language is suggested.

Furthermore, Claim 28 is absent.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 4, 21, 23, 37 and 39, drawn to a method for treating a respiratory tract of a mammal by aerosol administration of an effective amount of a composition comprising a sterically stabilized liposome carrier consisting of phosphatidylcholine and phosphatidylglycerol in combination with a drug, classified in class 424, subclass 450.
 - II. Claims 7-8, 24-25 and 40-41, drawn to a method for treating a respiratory tract of a mammal by aerosol administration of an effective amount of a composition comprising a sterically stabilized liposome carrier consisting of phosphatidylcholine and polyethylene glycol in combination with a drug, classified in class 424, subclass 450.
 - III. Claims 12, 29 and 45, drawn to a method for treating a respiratory tract of a mammal by aerosol administration of an effective amount of a composition comprising a sterically stabilized liposome carrier consisting of at least one of six specific combinations of compounds in combination with a drug, classified in class 424, subclass 450.
 - IV. Claims 13, 30 and 46, drawn to a method for treating a respiratory tract of a mammal by aerosol administration of an effective amount of a composition comprising a sterically stabilized liposome carrier consisting of a at least one of four specific combinations of compounds in combination with a drug, classified in class 424, subclass 450.

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Claims 1-3, 5-6, 9-11, 14-15, 18-20, 22, 26-27, 31-32, 35-36, 38, 42-44, 47-48 and 51-52 link Groups I-IV.

Claims 16 and 33 link Groups I, II and IV.

Claims 17, 34 and 49-50 link Groups I and IV.

Claims 1-3, 5-6, 9-11, 14-15, 18-20, 22, 26-27, 31-32, 35-36, 38, 42-44, 47-48 and 51-52 link Groups I-IV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), Claims 1-3, 5-6, 9-11, 14-15, 18-20, 22, 26-27, 31-32, 35-36, 38, 42-44, 47-48 and 51-52.

Claims 16 and 33 link Groups I, II and IV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), Claims 16 and 33.

Claims 17, 34 and 49-50 link Groups I and IV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), Claims 17, 34 and 49-50.

Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104. Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim(s) including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Groups I-IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, while each composition comprises a sterically stabilized liposome, each specified carrier molecule formulation is materially and structurally distinct from the others and confers distinctly different properties and effects on the liposome and its ability to interact with the target cell membrane. The carrier groups are essential inventive features of the sterically stabilized liposome, directly affecting the phase transition temperature and the bioavailability of the liposome. The distinctive carrier properties increase in complexity and uniqueness when non-obvious carrier compound subcombinations are intentionally combined into a final liposome composition.

Given that the intended use of the liposome carrier is to be compatible with a mammalian respiratory tract and to extend the effective life of a drug in the respiratory tract, the search and examination burden for all the different possible carrier compound combinations claimed to fulfill the recited functional requirements is exceptional. A search for phosphatidylinositol would not be co-extensive with a search for lipid-conjugated polysorbate. A reference rendering polyethylene glycol as anticipated or obvious over the prior art would not necessarily also render a lipid as anticipated or obvious over the prior art. Similarly, a finding that phosphatidylglycerol was novel and unobvious over the prior art would not necessarily extend to a finding that polyethylene glycol-distearoylphosphatidyl-diethanolamine with cholesterol was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated.

2. **Should Applicant elect any of Inventions I-IV**, a group restriction is required under 35 U.S.C. 121. Applicant is required to elect a single disclosed acyl group combination from the list of carriers recited specifically in Claims 9-11, 26-27, 42-44 for prosecution on the merits to which the claims shall be restricted. In the instant case, each acyl group is structurally distinct and confers distinctly different properties on the liposome carrier group. The specification

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teaches (page 6, lines 13-15 and page 8, lines 16-23) that the acyl groups are an essential inventive feature of the sterically stabilized liposome and directly affect the bioavailability of the liposome. A reference rendering a distearoyl as anticipated or obvious over the prior art would not necessarily also render plamitoyl oleoyl as anticipated or obvious over the prior art. Because a search of one acyl group combination does not necessarily overlap with that of another acyl group combination, it would be unduly burdensome for the examiner to search and examine all the acyl group combinations being sought in the presently pending claims for the reasons given above and thus, restriction for examination purposes as indicated.

Should Applicant elect Invention III, a further group restriction is required under 35 U.S.C. 121. Applicant is required to elect a single disclosed carrier combination from the list of carriers recited specifically in Claims 12, 29 and 45 for prosecution on the merits to which the claims shall be restricted.

Should Applicant elect Invention IV, a further group restriction is required under 35 U.S.C. 121. Applicant is required to elect a single disclosed carrier combination from the list of carriers recited specifically in Claims 13, 30 and 46 for prosecution on the merits to which the claims shall be restricted.

The carrier groups of Inventions III and IV are distinct for the same reasons given above. The carrier groups are essential inventive features of the sterically stabilized liposome, directly affecting the phase transition temperature and the bioavailability of the liposome. Because a search of one carrier combination does not necessarily overlap with that of another carrier combination, it would be unduly burdensome for the examiner to search and examine all the carrier combinations being sought in the presently pending claims for the reasons given above and thus, restriction for examination purposes as indicated.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed carrier combination for Inventions III and IV, even though this requirement is traversed. Failure to elect a specific carrier combination for Inventions III and IV consonant with Applicant's elected Invention, may result in a notice of non-responsive amendment.

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Should Applicant elect any of Inventions I-IV, further group restriction is required under 35 U.S.C. 121. Claim(s) 1-2, 14, 18-19, 35 and 47 are generic to a drug. Applicant is required to elect a single drug group, wherein illustrative drugs are recited specifically in Claim(s) 5-6, 15, 32, 48 and 51-52 for prosecution on the merits to which the claims shall be restricted. Therefore, election is required of any of Inventions I-V and one of the inventive drug groups (a)-(f) as described in Claims 15, 32 and 48.

- a) corticosteroids
- b) bronchodilators,
- c) leukotriene inhibitors,
- d) antihistamines,
- e) antibiotics,
- f) serine lung protease inhibitors,

The inventive drug groups (a)-(f) are distinct because,

The drugs of inventive drug groups (a)-(f) are unrelated. Each drug is materially and structurally distinct, and confers distinctly different properties and effects on the target cell. Furthermore, each drug is independent and mutually exclusive of the others. A reference rendering a corticosteroid as anticipated or obvious over the prior art would not necessarily also render an antibiotic as anticipated or obvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed drug, even though this requirement is traversed. Failure to elect a drug from Inventions I-V, inventive drug groups (a)-(f) above consonant with any of Applicant's elected Invention, may result in a notice of non-responsive amendment.

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3. **Should Applicant elect any of Inventions I-IV and any one of drug groups (a)-(f)** above, a species restriction is required under 35 U.S.C. 121. Currently, Claims 1, 18 and 35 of this application are generic to a plurality of disclosed, patentably distinct drug compounds that prohibit proper examination of this claim (see Claim 15, for example). Applicant is required under 35 U.S.C. 121 to elect one drug group (a)-(f) above and a single disclosed species from within the elected drug group in each claim for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

In the instant case, each drug species is materially and structurally distinct, as each drug confers distinctly different properties and effects on the target cell, and each drug is independent and mutually exclusive of the others. A search for terbutaline would not be co-extensive with a search for formoterol. A reference rendering montelukast as anticipated or obvious over the prior art would not necessarily also render zileuton as anticipated or obvious over the prior art. Similarly, a finding that rifamycin was novel and unobvious over the prior art would not necessarily extend to a finding that ciprofloxacin was also novel and unobvious over the prior art.

Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Failure to elect species consonant with Applicant's elected invention may result in a notice of non-responsive amendment.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

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4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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